

# PATENT COOPERATION TREATY

PCT

**NOTIFICATION OF ELECTION**  
**(PCT Rule 61.2)**

## From the INTERNATIONAL BUREAU

Date of mailing: 26 November 1998 (26.11.98)	in its capacity as elected Office
International application No.: PCT/GB98/01512	Applicant's or agent's file reference: P/2500.WOPAM
International filing date: 26 May 1998 (26.05.98)	Priority date: 23 May 1997 (23.05.97)
Applicant: CHOO, Yen et al	

- 1. The designated Office is hereby notified of its election made:**

in the demand filed with the International preliminary Examining Authority on:

14 October 1998 (14.10.98)

in a notice effecting later election filed with the International Bureau on:

2. The election  was

1

was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p><b>The International Bureau of WIPO</b>  <b>34, chemin des Colombettes</b>  <b>1211 Geneva 20, Switzerland</b></p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer:</p> <p>J. Zahra</p> <p>Telephone No.: (41-22) 338.83.38</p>
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**PCT****INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference  P2500WOP ATM	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No.  PCT/GB98/01512	International filing date (day/month/year)  26/05/1998	Priority date (day/month/year)  23/05/1997
International Patent Classification (IPC) or national classification and IPC  C12N15/10		
Applicant  MEDICAL RESEARCH COUNCIL et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I     Basis of the report
- II    Priority
- III    Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV    Lack of unity of invention
- V    Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI    Certain documents cited
- VII    Certain defects in the international application
- VIII    Certain observations on the international application

Date of submission of the demand  14/10/1998	Date of completion of this report  21.07.99
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. (+49-89) 2399-0 Tx: 523656 epmu d Fax: (+49-89) 2399-4465	Authorized officer  Morawetz, R  Telephone No. (+49-89) 2399 8155



**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/GB98/01512

**I. Basis of the report**

1. This report has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.*):

**Description, pages:**

1-44                   as originally filed

**Claims, No.:**

1-31                   as originally filed

**Drawings, sheets:**

1/8-8/8               as originally filed

2. The amendments have resulted in the cancellation of:

the description,       pages:  
 the claims,             Nos.:  
 the drawings,          sheets:

3.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

4. Additional observations, if necessary:

**II. Priority**

1.  This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
  - copy of the earlier application whose priority has been claimed.
  - translation of the earlier application whose priority has been claimed.
2.  This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid.

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Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.

**3. Additional observations, if necessary:**

**see separate sheet**

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- the entire international application.
- claims Nos. 1-27, 31.

because:

- the said international application, or the said claims Nos. 1-12 relate to the following subject matter which does not require an international preliminary examination (*specify*):

**see separate sheet**

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-27, 31 are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .

**IV. Lack of unity of invention**

**1. In response to the invitation to restrict or pay additional fees the applicant has:**

- restricted the claims.
- paid additional fees.
- paid additional fees under protest.
- neither restricted nor paid additional fees.

**INTERNATIONAL PRELIMINARY  
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2.  This Authority found that the requirement of unity of invention is not complied and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is
  - complied with.
  - not complied with for the following reasons:  
  
**see separate sheet**
4. Consequently, the following parts of the international application were the subject of international preliminary examination in establishing this report:
  - all parts.
  - the parts relating to claims Nos. .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Yes:	Claims
	No:	Claims 28-30
Inventive step (IS)	Yes:	Claims
	No:	Claims 28-30
Industrial applicability (IA)	Yes:	Claims 28-30
	No:	Claims

2. Citations and explanations

**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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**Re Item II**

Priority

1. In the absence of the priority document this preliminary report is being established under the assumption that the entire subject-matter is entitled to the claimed priority. If this is not the case the "P" document cited in the search report may have to be considered for novelty and/or inventive step. This document D1 (by the inventors) would be detrimental to most, if not all, of the claimed matter (Article 33(2), (3) PCT).

**Re Item III**

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. This authority is of the opinion that claims 1-27, 31 are so unclear, that no meaningful opinion can be formed on the novelty, inventive step or industrial applicability of the claimed invention (Article 34(4)(a)(ii) PCT)
- 1.1. Present claim 1 is directed to "a method for preparing a nucleic acid binding protein of the Cys2-His2 zinc finger class capable of binding to a nucleic acid quadruplet in a target nucleic acid sequence, wherein binding to base 4 of the quadruplet by an  $\alpha$ -helical zinc finger nucleic acid binding motif in the protein is determined as follows:
  - (a) if base 4 in the quadruplet is A, then position +6 in the  $\alpha$ -helix is Glu, Asn or Val ;
  - (b) if base 4 in the quadruplet is C, then position +6 in the  $\alpha$ -helix is Ser, Thr, Val, Ala, Glu or Asn".

Claim 1 does not meet the requirements of Article 6 PCT in that the matter for which protection is sought is not clearly defined. Said claim, although allegedly directed to a method for preparing a nucleic acid binding protein, does not define any technical features which relate to a method of preparing a protein, but only discloses a rule which defines 1 amino acid of an otherwise totally undefined protein.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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- 1.2. Present claims 2 - 27, 31 relate to further rules and methods for preparing a nucleic acid binding protein of the Cys2-His2 zinc finger class and to possible applications of the proteins. The same objection set out above, see 1.1, applies.
2. This authority is also of the opinion that claims 1-12, which relate to rules concerning the interaction of aminoacid residues of an  $\alpha$ -helical zinc finger nucleic acid binding motif with the different nucleotides of a quadruplet, concern subject matter on which it is not required to carry out an international preliminary examination (Article 34(4)(a)(i) and Rule 67.1(iii) PCT).

**Re Item IV**

Lack of unity of invention

Rule 13 PCT stipulates that the international application shall relate to one invention only or to a group so linked as to form a single general inventive concept. Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding "special technical features", i.e. technical features that define a novel and inventive contribution over the prior art.

The technical feature common to present claims 1-31 is, that they are concerned with nucleic acid binding proteins of the zinc finger class. Zinc finger proteins, methods to design them, applications thereof, etc. are, however, known in the prior art (see section V). Consequently, this common feature does not unitarily link the present set of claims and in the absence of another special technical feature, the present set of claims lacks an unifying concept and each nucleic acid binding protein prepared according to a different rule, its application, etc. is considered a separate invention.

**Re Item V**

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

International application No. PCT/GB98/01512

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents, the numbering corresponds to the listing of the documents in the international search report:

D1: Isalan, M. et al., PNAS 94: 5617-5621 (27 May 1997)

D2: WO 96 06166

The document D3 was not cited in the international search report. A copy of the document is appended hereto.

D3: Suzuki, M. et al., PNAS 91: 12357-12361 (1994)

2. The present application does not satisfy the criterion set forth in **Article 33(2) PCT** because the subject-matter of claims 28-30 is not new in respect of prior art as defined in the regulations (**Rule 64(1)-(3) PCT**).

Nucleic acid binding proteins, nucleic acids encoding them and transformed host cells are known from the prior art (see e.g. D2, D3). The design of the protein has no limiting scope on the protein, consequently, claims 28-30 are considered anticipated by the prior art.

3. The present application does not satisfy the criterion set forth in **Article 33(3) PCT** because its subject-matter, as understood from the description, does not involve an inventive step as defined in the regulations (**Rule 65 (1)-(2) PCT**) in view of the cited prior art (D2, D3).

- 3.1. Present application relates to rules describing the interaction of a zinc finger nucleic acid binding motif with the nucleotides of the bound nucleic acid and the application of said rules in the design of novel zinc finger proteins.

The rules disclosed in present application (page 7, line 14-page 8, line 1 and claims 1-3) determine the aminoacid residues of an  $\alpha$ -helical zinc finger nucleic acid binding motif according to the nucleotides present in the different positions of

the quadruplet.

Nucleic acid binding motifs for  $\alpha$ -helical zinc finger were originally defined as triplets (see, e.g. D2). The present application specifies overlapping quadruplets as binding motifs, such that, when read 3' to 5' on the -strand of the nucleic acid, base 4 of the first quadruplet is base 1 of the second and so on. Base 4 of the quadruplet is thus equivalent to the 5' base of the classical zinc finger binding triplet defined e.g. in D2 (see description, page 3, line 30 - page 4, line 3).

That zinc finger proteins recognize 4 base pairs and that the spacing type of the majority of ZnF proteins is T-1 [i.e., two neighbouring fingers share one base pair (-1) in a tandem arrangement] was known from the prior art (D3, page 12359, left hand column and Fig. 1e, 1f).

Rules which relate amino acids of an  $\alpha$ -helix to corresponding bases in the bound DNA triplet or quadruplet sequence are likewise known from D2 and D3, respectively.

D2 (Table 2) discloses a recognition code for amino acid-base contacts in interactions of an  $\alpha$ -helical zinc finger nucleic acid binding motif with DNA triplets. D2 furthermore discloses (page 35, line 9-28) that position +2 is able to specify the base directly 3' of the "cognate triplet" and can thus work in conjunction with position +6 of the preceding finger, which is basically the same information presented in present application (see page 4, line 10-14).

Table 2 of D2 explicitly discloses that if base 4 (= 5' base of D2) is G then position +6 in the  $\alpha$ -helix is Arg, if base 4 is T, then position +6 in the  $\alpha$ -helix is Ser or Thr and, thus, the rules set in present claims 2 and 3 a), c).

Table 2 of D2 furthermore discloses that if base 3 (= middle base of D2) is G, then position +3 in the  $\alpha$ -helix is His, if base 3 is A, then position +3 in the  $\alpha$ -helix is Asn, etc. and, thus, the rules set in claim 3 e)-3 j) and 3 l).

Figure 1 of D3 discloses that if base 4 is A, then position +6 in the  $\alpha$ -helix is Glu and if base 4 is C, then position +6 in the  $\alpha$ -helix is Glu, and thus the rules set in present claims 1 and 3 b), d).

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

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Summarising, most of the rules disclosed in the present application were either known from the prior art or could be easily derived from analysing further Zinc finger protein DNA interactions, according to the techniques disclosed in D2 and D3.

This authority is, thus, of the opinion, that the subject-matter of present application is devoid of any inventive merit.

**Re Item VII**

Certain defects

The attention of the applicants is drawn to the fact that for the assessment of claim 31 on the question whether it is industrially applicable, no unified criteria exist in the PCT.

09/424487

For receiving Office use only

## PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) P/2500.WOPAM

**Box No. I TITLE OF INVENTION**  
Nucleic Acid Binding proteins

**Box No. II APPLICANT**

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

Medical Research Council  
20 Park Crescent  
London  
W1N 4AL  
United Kingdom

 This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (i.e. country) of nationality:  
United Kingdom

State (i.e. country) of residence:  
United Kingdom

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

**Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)**

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

CHOO, Yen  
C/O MRC Laboratory of Molecular Biology  
Medical Research Council Centre  
Hills Road  
Cambridge  
CB2 2QH United Kingdom

This person is:

 applicant only applicant and inventor inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
GREECE

State (i.e. country) of residence:  
United Kingdom

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on a continuation sheet.

**Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

 agent common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

MASCHIO, Antonio  
D Young & Co  
21 New Fetter Lane  
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EC4A 1DA  
United Kingdom

Telephone No.

+44 1703 634816

Facsimile No.

+44 1703 224262

Teleprinter No.

477667 YOUNGS G

Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.

## Continuation of Box No. III FURTHER APPLICANTS AND/OR (FURTHER) INVENTORS

*If none of the following sub-boxes is used, this sheet is not to be included in the request.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

KLUG, Aaron  
C/O MRC Laboratory of Molecular Biology  
Medical Research Council Centre  
Hills Road  
Cambridge  
CB2 2QH  
United Kingdom

This person is:

- applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
United KingdomState (i.e. country) of residence:  
United Kingdom

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

ISALAN, Mark  
24 Shottfield Avenue  
East Sheen  
London  
SW14 8EA  
United Kingdom

This person is:

- applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:  
United KingdomState (i.e. country) of residence:  
United Kingdom

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

- applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below.)

This person is:

- applicant only  
 applicant and inventor  
 inventor only (If this check-box is marked, do not fill in below.)

State (i.e. country) of nationality:

State (i.e. country) of residence:

This person is applicant for the purposes of:  all designated States  all designated States except the United States of America  the United States of America only  the States indicated in the Supplemental Box

Further applicants and/or (further) inventors are indicated on another continuation sheet.

**Supplemental Box***If the Supplemental Box is not used, this sheet need not be included in the request.**Use this box in the following cases:*

- 1. If, in any of the Boxes, the space is insufficient to furnish all the information:**

*in particular:*

- (i) if more than two persons are involved as applicants and/or inventors and no "continuation sheet" is available;
- (ii) if, in Box No. II or in any of the sub-boxes of Box No. III, the indication "the States indicated in the Supplemental Box" is checked;
- (iii) if, in Box No. II or in any of the sub-boxes of Box No. III, the inventor or the inventor/applicant is not inventor for the purposes of all designated States or for the purposes of the United States of America;
- (iv) if, in addition to the agent(s) indicated in Box No. IV, there are further agents;
- (v) if, in Box No. V, the name of any State (or OAPI) is accompanied by the indication "patent of addition," or "certificate of addition," or if, in Box No. V, the name of the United States of America is accompanied by an indication "Continuation" or "Continuation-in-part";
- (vi) if there are more than three earlier applications whose priority is claimed;

- 2. If the applicant claims, in respect of any designated Office, the benefits of provisions of the national law concerning non-prejudicial disclosures or exceptions to lack of novelty:**

in such case, write "Continuation of Box No. ..." [indicate the number of the Box] and furnish the information in the same manner as required according to the captions of the Box in which the space was insufficient;

in such case, write "Continuation of Box No. III" and indicate for each additional person the same type of information as required in Box No. III. The country of the address indicated in this Box is the applicant's State (i.e. country) of residence if no State of residence is indicated below;

in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the applicant(s) involved and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is applicant;

in such case, write "Continuation of Box No. II" or "Continuation of Box No. III" or "Continuation of Boxes No. II and No. III" (as the case may be), indicate the name of the inventor(s) and, next to (each) such name, the State(s) (and/or, where applicable, ARIPO, Eurasian, European or OAPI patent) for the purposes of which the named person is inventor;

in such case, write "Continuation of Box No. IV" and indicate for each further agent the same type of information as required in Box No. IV;

in such case, write "Continuation of Box No. V" and the name of each State involved (or OAPI), and after the name of each such State (or OAPI), the number of the parent title or parent application and the date of grant of the parent title or filing of the parent application;

in such case, write "Continuation of Box No. VI" and indicate for each additional earlier application the same type of information as required in Box No. VI.

in such case, write "Statement Concerning Non-Prejudicial Disclosures or Exceptions to Lack of Novelty" and furnish that statement below.

CONTINUATION OF BOX IV - ADDITIONAL REPRESENTATIVES

PURVIS, William Michael Cameron  
 COTTER, Ivan John  
 PILCH, Adam John Michael  
 CRISP, David Norman  
 ROBINSON, Nigel Alexander Julian  
 HARRIS, Ian Richard  
 TURNER, James Arthur  
 HARDING, Charles Thomas  
 MALLALIEU, Catherine Louise  
 PRICE, Paul Anthony King  
 PRATT, Richard Wilson  
 HOLMES, Miles Keeton  
 HORNER, David  
 NACHSHEN, Neil  
 POTTER, Julian Mark

**Box No.V DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

**Regional Patent**

- AP ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SZ Swaziland, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- EA Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- EP European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- OA OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

**National Patent (if other kind of protection or treatment desired, specify on dotted line):**

- |  |  |
|--|--|
| <input checked="" type="checkbox"/> AL Albania .....                               | <input checked="" type="checkbox"/> LT Lithuania .....                                 |
| <input checked="" type="checkbox"/> AM Armenia .....                               | <input checked="" type="checkbox"/> LU Luxembourg .....                                |
| <input checked="" type="checkbox"/> AT Austria .....                               | <input checked="" type="checkbox"/> LV Latvia .....                                    |
| <input checked="" type="checkbox"/> AU Australia .....                             | <input checked="" type="checkbox"/> MD Republic of Moldova .....                       |
| <input checked="" type="checkbox"/> AZ Azerbaijan .....                            | <input checked="" type="checkbox"/> MG Madagascar .....                                |
| <input checked="" type="checkbox"/> BA Bosnia and Herzegovina .....                | <input checked="" type="checkbox"/> MK The former Yugoslav Republic of Macedonia ..... |
| <input checked="" type="checkbox"/> BB Barbados .....                              | <input checked="" type="checkbox"/> MN Mongolia .....                                  |
| <input checked="" type="checkbox"/> BG Bulgaria .....                              | <input checked="" type="checkbox"/> MW Malawi .....                                    |
| <input checked="" type="checkbox"/> BR Brazil .....                                | <input checked="" type="checkbox"/> MX Mexico .....                                    |
| <input checked="" type="checkbox"/> BY Belarus .....                               | <input checked="" type="checkbox"/> NO Norway .....                                    |
| <input checked="" type="checkbox"/> CA Canada .....                                | <input checked="" type="checkbox"/> NZ New Zealand .....                               |
| <input checked="" type="checkbox"/> CH and LI Switzerland and Liechtenstein .....  | <input checked="" type="checkbox"/> PL Poland .....                                    |
| <input checked="" type="checkbox"/> CN China .....                                 | <input checked="" type="checkbox"/> PT Portugal .....                                  |
| <input checked="" type="checkbox"/> CU Cuba .....                                  | <input checked="" type="checkbox"/> RO Romania .....                                   |
| <input checked="" type="checkbox"/> CZ Czech Republic .....                        | <input checked="" type="checkbox"/> RU Russian Federation .....                        |
| <input checked="" type="checkbox"/> DE Germany .....                               | <input checked="" type="checkbox"/> SD Sudan .....                                     |
| <input checked="" type="checkbox"/> DK Denmark .....                               | <input checked="" type="checkbox"/> SE Sweden .....                                    |
| <input checked="" type="checkbox"/> EE Estonia .....                               | <input checked="" type="checkbox"/> SG Singapore .....                                 |
| <input checked="" type="checkbox"/> ES Spain .....                                 | <input checked="" type="checkbox"/> SI Slovenia .....                                  |
| <input checked="" type="checkbox"/> FI Finland .....                               | <input checked="" type="checkbox"/> SK Slovakia .....                                  |
| <input checked="" type="checkbox"/> GB United Kingdom .....                        | <input checked="" type="checkbox"/> SL Sierra Leone .....                              |
| <input checked="" type="checkbox"/> GE Georgia .....                               | <input checked="" type="checkbox"/> TJ Tajikistan .....                                |
| <input checked="" type="checkbox"/> GH Ghana .....                                 | <input checked="" type="checkbox"/> TM Turkmenistan .....                              |
| <input checked="" type="checkbox"/> GM Gambia .....                                | <input checked="" type="checkbox"/> TR Turkey .....                                    |
| <input checked="" type="checkbox"/> GW Guinea-Bissau .....                         | <input checked="" type="checkbox"/> TT Trinidad and Tobago .....                       |
| <input checked="" type="checkbox"/> HU Hungary .....                               | <input checked="" type="checkbox"/> UA Ukraine .....                                   |
| <input checked="" type="checkbox"/> ID Indonesia .....                             | <input checked="" type="checkbox"/> UG Uganda .....                                    |
| <input checked="" type="checkbox"/> IL Israel .....                                | <input checked="" type="checkbox"/> US United States of America .....                  |
| <input checked="" type="checkbox"/> IS Iceland .....                               | <input checked="" type="checkbox"/> UZ Uzbekistan .....                                |
| <input checked="" type="checkbox"/> JP Japan .....                                 | <input checked="" type="checkbox"/> VN Viet Nam .....                                  |
| <input checked="" type="checkbox"/> KE Kenya .....                                 | <input checked="" type="checkbox"/> YU Yugoslavia .....                                |
| <input checked="" type="checkbox"/> KG Kyrgyzstan .....                            | <input checked="" type="checkbox"/> ZW Zimbabwe .....                                  |
| <input checked="" type="checkbox"/> KP Democratic People's Republic of Korea ..... |  |
| <input checked="" type="checkbox"/> KR Republic of Korea .....                     |  |
| <input checked="" type="checkbox"/> KZ Kazakhstan .....                            |  |
| <input checked="" type="checkbox"/> LC Saint Lucia .....                           |  |
| <input checked="" type="checkbox"/> LK Sri Lanka .....                             |  |
| <input checked="" type="checkbox"/> LR Liberia .....                               |  |
| <input checked="" type="checkbox"/> LS Lesotho .....                               |  |

Check-boxes reserved for designating States (for the purposes of a national patent) which have become party to the PCT after issuance of this sheet:

- CYPRUS (in respect of the EP designation)
- 
- 

In addition to the designations made above, the applicant also makes under Rule 4.9(b) all designations which would be permitted under the PCT except the designation(s) of \_\_\_\_\_.

The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation of a designation consists of the filing of a notice specifying that designation and the payment of the designation and confirmation fees. Confirmation must reach the receiving Office within the 15-month time limit.)

**Box No. VI PRIORITY CLAIM**Further priority claims are indicated in the Supplemental Box 

The priority of the following earlier application(s) is hereby claimed:

Country (in which, or for which, the application was filed)	Filing Date (day/month/year)	Application No.	Office of filing (only for regional or international application)
item (1) United Kingdom	23.05.97	9710809.6	
item (2)			
item (3)			

Mark the following check-box if the certified copy of the earlier application is to be issued by the Office which for the purposes of the present international application is the receiving Office (a fee may be required):

The receiving Office is hereby requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) identified above as item(s): (1)

**Box No. VII INTERNATIONAL SEARCHING AUTHORITY**

Choice of International Searching Authority (ISA) (If two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used): ISA /

Earlier search Fill in where a search (international, international-type or other) by the International Searching Authority has already been carried out or requested and the Authority is now requested to base the international search, to the extent possible, on the results of that earlier search. Identify such search or request either by reference to the relevant application (or the translation thereof) or by reference to the search request:

Country (or regional Office): Date (day/month/year): Number:

**Box No. VIII CHECK LIST**

This international application contains the following number of sheets:

- 1. request : 5 sheets
  - 2. description : 44 sheets
  - 3. claims : 6 sheets
  - 4. abstract : 1 sheets
  - 5. drawings : 10 sheets
- Total : 66 sheets

This international application is accompanied by the item(s) marked below:

- 1.  separate signed power of attorney
- 2.  copy of general power of attorney
- 3.  statement explaining lack of signature
- 4.  priority document(s) identified in Box No. VI as item(s):
- 5.  fee calculation sheet
- 6.  separate indications concerning deposited microorganisms
- 7.  nucleotide and/or amino acid sequence listing (diskette)
- 8.  other (specify):

Figure No. \_\_\_\_\_ of the drawings (if any) should accompany the abstract when it is published.

**Box No. IX SIGNATURE OF APPLICANT OR AGENT**

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request):

A MASCHIO

For receiving Office use only

1. Date of actual receipt of the purported international application:

3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:

4. Date of timely receipt of the required corrections under PCT Article 11(2):

5. International Searching Authority specified by the applicant: ISA /

2. Drawings:

 received: not received:6.  Transmittal of search copy delayed until search fee is paid

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

4-6-98

*This sheet is not part of and does not count as a sheet of the international application.***PCT****FEE CALCULATION SHEET**  
**Annex to the Request**

For receiving Office use only

International application No.

Applicant's or agent's  
file reference P/2500.WOPAM

Date stamp of the receiving Office

Applicant  
MEDICAL RESEARCH COUNCIL**CALCULATION OF PRESCRIBED FEES**

1. TRANSMITTAL FEE . . . . . £ 55.00 T
2. SEARCH FEE . . . . . £ 780.00 S

International search to be carried out by \_\_\_\_\_  
(If two or more International Searching Authorities are competent in relation to the international application, indicate the name of the Authority which is chosen to carry out the international search.)

3. INTERNATIONAL FEE

## Basic Fee

The international application contains 66 sheets.

first 30 sheets . . . . . £285.00 b<sub>1</sub>36 x £6 = £216.00 b<sub>2</sub>

remaining sheets additional amount

Add amounts entered at b<sub>1</sub> and b<sub>2</sub> and enter total at B . . . . . £501.00 B

## Designation Fees

The international application contains 75 designations.

11 x £65 = £715.00 D

number of designation fees amount of designation fee payable (maximum 11)

Add amounts entered at B and D and enter total at I . . . . . £1,216.00 I

(Applicants from certain States are entitled to a reduction of 75% of the international fee. Where the applicant is (or all applicants are) so entitled, the total to be entered at I is 25% of the sum of the amounts entered at B and D.)

4. FEE FOR PRIORITY DOCUMENT . . . . .

£ 22.00 P

5. TOTAL FEES PAYABLE

Add amounts entered at T, S, I and P, and enter total in the TOTAL box . . . . .

£2,073.00

TOTAL

 The designation fees are not paid at this time.**MODE OF PAYMENT**

<input checked="" type="checkbox"/>	authorization to charge deposit account (see below)
<input type="checkbox"/>	cheque
<input type="checkbox"/>	postal money order

<input type="checkbox"/>	bank draft
<input type="checkbox"/>	cash
<input type="checkbox"/>	revenue stamps

<input type="checkbox"/>	coupons
<input type="checkbox"/>	other (specify): _____

**DEPOSIT ACCOUNT AUTHORIZATION** (this mode of payment may not be available at all receiving Offices)The RO/ UKPO  is hereby authorized to charge the total fees indicated above to my deposit account. is hereby authorized to charge any deficiency or credit any overpayment in the total fees indicated above to my deposit account. is hereby authorized to charge the fee for preparation and transmittal of the priority document to the International Bureau of WIPO to my deposit account.002246  
Deposit Account Number4 June 1998  
Date (day/month/year)ANTONIO MASCHIO  
Signature

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>P/2500.WOPAM</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/GB 98/01512</b>	International filing date (day/month/year) <b>26/05/1998</b>	(Earliest) Priority Date (day/month/year) <b>23/05/1997</b>
Applicant <b>MEDICAL RESEARCH COUNCIL et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1.  Certain claims were found unsearchable (see Box I).
2.  Unity of invention is lacking (see Box II).
3.  The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
  - filed with the international application.
  - furnished by the applicant separately from the international application,
    - but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
  - Transcribed by this Authority
4. With regard to the title,  the text is approved as submitted by the applicant
  - the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - the text is approved as submitted by the applicant
  - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this International Search Report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:
 

Figure No. 1b  as suggested by the applicant.  None of the figures.

  - because the applicant failed to suggest a figure.
  - because this figure better characterizes the invention.

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/GB 98/01512

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 31  
because they relate to subject matter not required to be searched by this Authority, namely:

**Remark:** Although claim 31  
is directed to a method of treatment of the human/animal  
body, the search has been carried out and based on the alleged  
effects of the compound/composition.

2.  Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such  
an extent that no meaningful International Search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all  
searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment  
of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report  
covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is  
restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

09/424487

Int'l Application No  
PCT/GB 98/01512

A. CLASSIFICATION OF SUBJECT MATTER

IPC 6 C12N15/10	C12N15/12	C12N15/62	C12Q1/68	C07K14/47
A61K48/00				

According to International Patent Classification(IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 6 C12N C12Q C07K A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P, A	M. ISALAN ET AL: "Synergy between adjacent zinc fingers in sequence-specific DNA recognition" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, vol. 94, 27 May 1997, pages 5617-5621, XP002075337 WASHINGTON US see the whole document ---	
A	WO 96 06166 A (MEDICAL RES COUNCIL ;CHOO YEN (SG); KLUG AARON (GB); GARCIA ISIDRO) 29 February 1996 cited in the application see the whole document see figure 1D -----	

 Further documents are listed in the continuation of box C. Patent family members are listed in annex.

## \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

1 September 1998

30/09/1998

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Cervigni, S

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT/GB 98/01512

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9606166 A	29-02-1996	AU 3229195 A		14-03-1996
		CA 2196419 A		29-02-1996
		EP 0781331 A		02-07-1997
		JP 10504461 T		06-05-1998

## PATENT COOPERATION TREATY

09/424487

PCT

From the INTERNATIONAL BUREAU

To:

MASCHIO, Antonio  
 D. Young & Co.  
 21 New Fetter Lane  
 London EC4A 1DA  
 ROYAUME-UNI

*Records noted DS ATM*

Date of mailing (day/month/year)  
 06 October 1999 (06.10.99)

Applicant's or agent's file reference  
 P/2500.WOPAM

## IMPORTANT NOTIFICATION

International application No.  
 PCT/GB98/01512

International filing date (day/month/year)  
 26 May 1998 (26.05.98)

1. The following indications appeared on record concerning:

the applicant     the inventor     the agent     the common representative

Name and Address

MEDICAL RESEARCH COUNCIL  
 20 Park Crescent  
 London W1N 4AL  
 United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Faximile No.

Teleprinter No.

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person     the name     the address     the nationality     the residence

Name and Address

GENDAQ LIMITED  
 1-3 Burtonhole Lane  
 Mill Hill  
 London NW7 1AD  
 United Kingdom

State of Nationality

GB

State of Residence

GB

Telephone No.

Faximile No.

Teleprinter No.

3. Further observations, if necessary:

4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO  
 34, chemin des Colombettes  
 1211 Geneva 20, Switzerland

Authorized officer

*Karl Huynh-Khuong*

Facsimile No.: (41-22) 740.14.35

Telephone No.: (41-22) 338.83.38



**CERTIFICATE OF INCORPORATION  
ON CHANGE OF NAME**

Company No. 3756817

The Registrar of Companies for England and Wales hereby certifies that  
**ENDLOCK LIMITED**

having by special resolution changed its name, is now incorporated  
under the name of  
**GENDAQ LIMITED**

Given at Companies House, Cardiff, the 24th June 1999



THE OFFICIAL SEAL OF THE  
REGISTRAR OF COMPANIES



**C O M P A N I E S   H O U S E**

## PATENT ASSIGNMENT

DATE: 21 MAY 1999

### PARTIES:

- (1) MEDICAL RESEARCH COUNCIL (a body incorporated by Royal Charter) of 20 Park Crescent, London WIN 4AL, England ("Assignor")
- (2) ENDLOCK LIMITED (Registered in England No. 3756817) whose registered office is at 90 Long Acre, London WC2E 9TT, England ("Assignee")

### RECITALS:

- (A) The ASSIGNOR is the applicant in respect of the patent applications named in the Schedule to this Assignment (the "Applications") in respect of the inventions disclosed in the Applications (the "Inventions").
- (B) The parties have agreed that all the Assignor's rights in the Applications and the Inventions shall be assigned to the Assignee.

### OPERATIVE TERMS:

In consideration of the sum of £1,450 paid by the Assignee to the Assignor (the receipt and sufficiency of which is hereby acknowledged) IT IS AGREED as follows:

#### I. Assignment

The Assignor hereby assigns to the Assignee throughout the world:

- (a) the Inventions and all right and title of the Assignor therein;
- (b) the Applications and all patent applications, patents and supplementary protection certificates which may derive or result from any of the same, including any divisionals, continuations, reissues, extensions and registrations in relation to any thereof and all and any other rights in the inventions comprised in the above (together referred to as the "Patent Rights");
- (c) the benefit of all priority dates;
- (d) its right to apply for and obtain patents, registrations or similar forms of protection in other countries in respect of the Inventions or otherwise included in or derived from the Patent Rights;
- (e) its right to make any new application(s) in respect of any parts of the subject matter of any application or specification filed in connection with the Inventions and the right to claim priority from the Applications;

(f) its right to sue for and obtain injunctive relief, damages and all other relief in respect of any infringement or misuse (whether past present or future) of the Applications or of the rights conferred by publication of the same or of any other of the Patent Rights.

2. Validity

The Assignor has made available to the Assignee its case information concerning the current state and progress of the Applications but nothing in this Assignment shall be construed as a representation or warranty that any of the Applications will proceed to grant or that any of the Patent Rights are valid or that any exploitation of the Inventions represented by the Applications will not be an infringement of any patents or other rights not vested in the Assignor.

3. Further Assurance

The Assignor agrees at the request and expense of the Assignee to execute any further documents and do all things which the Assignee may reasonably require in order to vest in the Assignee (or the Assignee's successors in title or nominees as the case may be) the Patent Rights including the Applications and all other rights title and interests intended to be assigned transferred or granted to the Assignee hereunder and to give the Assignee the full benefit of this Assignment including doing all acts which may be necessary or desirable to record the Applications and any other Patent Rights in the name of the Assignee in any relevant register of patent rights.

4. Law

This Assignment shall be governed by and construed and take effect in accordance with English law.

IN WITNESS of which the parties have executed this Assignment on the date shown at the beginning of this Assignment.

SCHEDULE

Number

PCT/GB95/01949	(granted in Australia, but pending elsewhere)
PCT/GB98/01510	
PCT/GB98/01512	
PCT/GB98/01514	
PCT/GB98/01516	
GB:980 5576.7	
GB:980 6895.0	
GB: 980 7246.5	

EXECUTED for and on behalf of  
MEDICAL RESEARCH COUNCIL

Signature: 

Name: Graham L. Wagner  
Licensing and Agreements Manager

Title: .....

EXECUTED for and on behalf of  
ENDLOCK LIMITED

Signature: 

Name: Stephen T. Reede

Title: Director